REMARKS

Status of the Claims

Pending claims

Claims 1 to 7 as filed are pending.

Claims amended and added in the instant amendment

Claims 1 to 4 and 7, are canceled, without prejudice, claims 5 and 6 are amended, claims 8 to 27 are added. Thus, after entry of the instant amendment, claims 5, 6 and 8 to 27 will be pending and under consideration.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to methods for culturing a cell, wherein the method comprises culturing the cell using a carrier for cell culture and the carrier comprises a porous membrane and an alginate gel layer which is formed on the porous membrane, where the porous membrane is not permeable to alginate gel, can be found, inter alia, on page 4, lines 16 to 17. Support for claims directed to calcium alginate gels can be found, inter alia, on page 3, line 22. Support for claims directed to methods wherein the carrier further comprises an extracellular matrix component gel layer or extracellular matrix component sponge layer which is formed on the alginate gel layer can be found, inter alia, on page 3, lines 23 to 25. Support for claims directed to methods wherein the extracellular matrix component comprises a collagen can be found, inter alia, on page 3, line 26. Support for claims directed to methods further comprising forming a cell multi-layer can be found, inter alia, on page 4, line 5. Support for claims directed to methods wherein the porous membrane comprises a filter, an ultrafiltration membrane, a silicone rubber membrane, a polytetrafluoroethylene resin porous membrane, a nonwoven fabric or a gauze-like mesh can be found, inter alia, on page 3, lines 20 to 24. Support for claims directed to methods wherein the porous membrane comprises pores can be found, inter alia, on page 3, lines 24 to 26. Support for claims directed to methods for making a three-dimensional tissue structure can be found, inter alia, on page 10, lines 5 to 9. Support for claims directed to methods for *in vitro* drug permeability testing can be found, inter alia, on page 10, lines 7 to 9.

Applicant : Hara, et al.
Serial No. : 09/699,133
Filed : October 27, 2000
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Attorney's Docket No.: 13781-002001 / PH-1074US

The Restriction Requirement

The Patent Office has alleged that the pending claims of the application are directed to three separate and distinct inventions under 35 U.S.C. §121, as follows:

Group I: Claims 1 to 4, drawn to a carrier for cell culture.

Group II: Claims 5 to 6, drawn to a process of culturing a cell.

Group III: Claim 7, drawn to a multi-layer cell product.

The Election

In response to the Restriction Requirement, Applicants elect Group II, claims 5 to 6, drawn to the embodiment of a process of culturing a cell. The election is made without traverse.

If an additional fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 06-1050. Please credit any overpayment to the above-noted Deposit Account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858 678 5070.

Respectfully submitted,

Date: April 19, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Applicant : Hara, et al. Art Unit : 1651
Serial No. : 09/699,133 Examiner : David Naff
Filed : October 27, 2000
Title : CARRIERS FOR CELL CULTURE AND METHODS FOR CULTURING CELLS USING THE SAME

In The Claims:

Claims 1 to 4 and 7 have been canceled, without prejudice.

Claims 5 and 6 have been amended as follows:

5. (Amended) A method for culturing a cell, wherein the method comprises culturing the cell using [the] a carrier for cell culture [according to any one of claims claim 1 to 4], wherein the carrier for cell culture comprises a porous membrane and an alginate gel layer which is formed on the porous membrane,

wherein the porous membrane is not permeable to alginate gel.

6. (Amended) A method for piling up a cell, wherein the method comprises:

(a) forming a cell layer on [the] a carrier [according to any one of claims 1 to 4];

wherein the carrier comprises a porous membrane and an alginate gel layer which is formed on the porous membrane;

(b) solubilizing an alginate gel layer of the carrier thereby exfoliating the cell layer from a porous membrane of the carrier; and

(c) piling up the exfoliated cell layer on another cell formed on the carrier [according to any one of claims claim 1 to 4].

The following new claims have been added:

8. (NEW) The method of claim 5 or claim 6, wherein the alginate gel layer is composed of a calcium alginate gel.

9. (NEW) The method of claim 5 or claim 6, wherein the carrier further comprises an extracellular matrix component gel layer or extracellular matrix component (ECM) sponge layer which is formed on the alginate gel layer.

10. (NEW) The method of claim 5 or claim 6, wherein the extracellular matrix component comprises a collagen.

11. (NEW) The method of claim 5, further comprising forming a cell multi-layer.

12. (NEW) The method of claim 5 or claim 6, wherein the porous membrane comprises a filter, an ultrafiltration membrane, a silicone rubber membrane, a polytetrafluoroethylene resin porous membrane, a nonwoven fabric or a gauze-like mesh.

13. (NEW) The method of claim 5 or claim 6, wherein the porous membrane comprises pores.

14. (NEW) The method of claim 13, wherein the pores are between about 0.02 to 1000 μm.

15. (NEW) The method of claim 9, wherein the extracellular matrix component comprises a collagen, an elastin, a proteoglycan, a glucosaminoglycan, a fibronectin, a laminin, a vitronectin or a heparan sulfate.

16. (NEW) The method of claim 9, wherein the extracellular matrix component comprises a gel comprising collagen type IV, laminin and heparan sulfate.

17. (NEW) The method of claim 5 or claim 6, wherein the thickness of the porous membrane is between about 0.01 to 1 mm, 0.01 to 0.1 mm, or 0.05 to 1 mm.

18. (NEW) The method of claim 5 or claim 6, wherein the thickness of the alginate gel layer is between about 0.1 to 3 mm, 1 to 2 mm, or about 1 mm.

19. (NEW) The method of claim 9, wherein the extracellular matrix component gel layer is between about 0.1 to 1 mm, 0.2 to 0.5 mm, or about 0.4 mm.

20. (NEW) The method of claim 9, wherein the thickness of the extracellular matrix component sponge layer is between about 0.1 to 2 mm, 0.2 to 1 mm, or about 0.5 mm.

21. (NEW) The method of claim 5 or claim 6, wherein the cell is a fibroblast, a vascular endothelial cell, a chondrocyte, a hepatocyte, a small intestine epitheliocyte, an epidermis cornification cell, an osteoblast, a bone marrow mesenchymal cell or a fibroblast.

22. (NEW) The method of claim 5 or claim 6, wherein a cell concentration of between about 10,000 to 15,000 cells/ml is added onto the alginate gel layer.

22. (NEW) The method of claim 5 or claim 6, further comprising detaching the cells from the porous membrane by solubilizing the alginate gel layer.

23. (NEW) The method of claim 22, wherein solubilization of the alginate gel layer is carried out by use of a chelating agent.

24. (NEW) The method of claim 23, wherein the chelating agent comprises a polyaminocarboxylic acid, an ethylenediaminetetraacetic acid, an ethylene glycol-bis(β-aminoethyl ether), an oxycarboxylic acids, or a citric acid.

25. (NEW) A method for making a three-dimensional tissue structure comprising the following steps:

(a) forming a cell layer on a carrier, wherein the carrier comprises a porous membrane and an alginate gel layer which is formed on the porous membrane;

(b) solubilizing an alginate gel layer of the carrier thereby exfoliating the cell layer from a porous membrane of the carrier; and

(c) piling up the exfoliated cell layer on another cell formed on the carrier, thereby making a three-dimensional tissue structure.

26. (NEW) A method for making a three-dimensional tissue structure comprising culturing a cell using a carrier for cell culture, wherein the carrier for cell culture comprises a porous membrane and an alginate gel layer which is formed on the porous membrane, wherein the porous membrane is not permeable to alginate gel.

27. (NEW) A method for *in vitro* drug permeability testing comprising culturing a cell using a carrier for cell culture, wherein the carrier for cell culture comprises a porous membrane and an alginate gel layer which is formed on the porous membrane, wherein the porous membrane is not permeable to alginate gel.